803 Blockade of Tissue Proliferation After Coronary Interventions

Wednesday, March 19, 1997, 4:00 p.m.–5:00 p.m.
Anaheim Convention Center, Room A1

4:00

803-1 Impact of Cilostazol on Intimal Proliferation Following Directional Coronary Atherectomy: A Prospective Randomized Trial

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Cilostazol, a new synthetic platelet-aggregation inhibitor, has a specific inhibitory action on cyclic AMP phosphodiesterase. It inhibits intimal proliferation of injured carotid artery of rats or stented iliac artery of dogs as a result of cyclic AMP accumulation in smooth muscle cells. The aim of this study was to determine the effect of cilostazol on intimal proliferation following directional coronary atherectomy. Thirty nine patients with lesions suitable for DCA were randomized to a cilostazol (C) (200 mg/day) group (20 pts) or an aspirin (A) (250 mg/day) group (19 pts). Medication was started 1 week before DCA and was continued to follow-up in all patients. Serial QCA and IVUS was performed at pre-, post-DCA and follow-up (Fu). Mean Fu duration was 209 ± 38 days. QCA was performed by a Cardiovascular Measurement System. Angiographic restenosis was defined as a % diameter stenosis ≥50% at Fu. Vessel area (VA) and plaque area (PA) were measured serially at the narrowest site in the lesion at pre-DCA. QCA and QCU were performed blindly. QCA and QCU data were as follows:

QCA	preRD	preMLD	postMLD	Fu MLD	Fu % DS	Restenosis
C group	3.04 mm	0.89 mm	2.81 mm	2.33 mm*	25%*	0%*
A group	3.16 mm	0.83 mm	2.77 mm	1.81 mm	41%	26%

QCU	preVA	postPA	post % PA	Fu PA	Fu % PA	dPA
C group	15.5 mm^2	8.2 mm^2	47%	8.7 mm^2	56%*	0.5 mm^2
A group	16.0 mm^2	9.1 mm^2	48%	10.9 mm^2	64%	1.8 mm^2

*$p < 0.05$ vs A group (RD = reference diameter, MLD = minimal lumen diameter, DS = diameter stenosis, dPA = Fu PA-postPA)

Conclusion: Cilostazol has an inhibitory effect on intimal proliferation following DCA and significantly reduces restenosis.

4:15

803-2 Late Tissue Proliferation *Both* Within and Surrounding Palmaz-Schatz Stents is Associated with Procedural Vessel Wall Injury

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Previous serial intravascular ultrasound studies have shown that Palmaz-Schatz stent implantation induces both in-stent and peri-stent tissue proliferation. To determine whether these are a function of vessel wall injury, we studied 90 native vessel lesions using post-intervention and follow-up (F/U) ultrasound {measurement of arterial, stent, and lumen areas (mm^2) and calculation of % in-stent intimal hyperplasia (% IH = stent-lumen/stent) area, peri-stent plaque (arterial-stent) area, and peri-stent tissue growth (Δperi-stent plaque area)} and quantitative angiography (measurement of loss index = late loss/acute gain). An injury score (IS) was constructed from procedural variables: **0** (adjunct PTCA pressure ≤ 16 atm & balloon:artery ratio ≤ 1.1), **1** (adjunct PTCA pressure >16 atm *or* balloon:artery ratio >1.1, and **2** (adjunct PTCA pressure >16 atm & balloon:artery ratio >1.1).

	IS = 0 (N = 17)	IS = 1 (N = 58)	IS = 2 (N = 15)	p ANOVA
F/U lumen area	3.7 ± 3.1	2.8 ± 2.2	1.3 ± 0.6	0.0037
F/U % IH area	51 ± 22	54 ± 21	61 ± 14	0.0627
Peri-stent tissue growth	1.1 ± 1.2	1.5 ± 1.4	2.5 ± 1.1	0.0322
Loss index	0.7 ± 0.4	0.9 ± 0.4	1.3 ± 1.4	0.0290

Peri-stent tissue growth correlated with in-stent IH ($p = 0.0121$). Both peri-stent tissue growth (1.9 ± 1.4 vs 1.3 ± 1.0, $p = 0.0640$) and in-stent IH (4.0 ± 21. vs 1.2 ± 0.7, $p < 0.0001$) were greater in restenotic than in non-restenotic stents. *We conclude:* Deep vessel wall injury as a result of oversized stents implanted at high (>16 atm) pressures results in exaggerated in-stent and peri-stent tissue growth. This manifests as reduced F/U lumen areas and increased in-stent restenosis.

4:30

803-3 ACE Inhibition Accelerates Endothelial Regrowth in Vivo: A Possible Explanation for the Benefit Observed with ACE Inhibitors Following Arterial Injury

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Recent *in vitro* studies suggest that angiotensin converting enzyme (ACE) inhibitors stimulate endothelial cell proliferation and migration. The present study was designed to test the hypothesis that an ACE inhibitor may accelerate endothelial regrowth *in vivo*. Twenty four New Zealand White rabbits were randomized to receive orally placebo or the ACE inhibitor perindopril (1 mg/kg/day) and underwent balloon denudation of one iliac artery 7 days later. At the time of vascular injury plasma ACE activity was effectively blocked in ACE inhibitor treated animals compared to controls (5.2 ± 2.8 mU/mL versus 93.7 ± 6.4 mU/mL; $P < 0.0001$). Twenty eight days after injury, animals were sacrificed and endothelial regrowth was evaluated by planimetric quantification of the non-stained luminal surface following injection of Evans blue. Reendothelialization was significantly greater in ACE inhibitor treated animals than in controls (131 ± 9 mm^2 versus 69 ± 8 mm^2; $P < 0.001$). Analysis of percent reendothelialization, defined as the ratio of the reendothelialized area divided by the initially denuded area (× 100), confirmed these results (73 ± 3% versus 37 ± 3%, $P < 0.0001$). These results were validated by performing scanning electron microscopy and specific immunostaining for endothelial cells (PECAM-1).

Conclusions: These data provide the first *in vivo* demonstration that ACE inhibitors accelerate endothelial regrowth after arterial injury. This effect may contribute to the benefit observed with ACE inhibition following arterial injury.

4:45

803-4 Radiotherapy Reduces Coronary Restenosis: Late Follow-Up

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The SCRIPPS (Scripps Coronary Radiation to Inhibit Proliferation Post-Stenting) trial is a double-blind, randomized, placebo-controlled trial of intracoronary gamma (Ir-192) radiation plus stenting in pts with previous restenosis. Fifty-five pts were enrolled from 3/24/95 to 12/22/95. Angiographic follow-up (FU) was obtained on all eligible pts at 6.7 ± 2.2 mos (range 2–14). Independent, quantitative core lab analysis revealed:

	Ir-192 (n = 24)†	Placebo (n = 28)‡	P
Reference diameter (mm)	2.88	2.78	NS
% stenosis, pre	61.5	62.2	NS
% stenosis, post	2.82	2.87	NS
% stenosis, FU	17	37	0.01
FU lumen diameter (mm)	2.43	1.85	0.02
Late lumen loss (mm)	0.38	1.03	0.02
Late loss index (mm)	0.12	0.60	0.002

†1 stent thrombosis; 1 angiogram unanalyzable, ‡1 cardiac death at 8 months

Late clinical follow-up is available for 100% of pts at 12.3 ± 2.9 mos (range 8–18). There was 1 cardiac death (placebo) and 1 stent thrombosis (Ir-192) resulting in non-Q-wave MI. Target lesion revascularization was required in 16 (29%) pts (Ir-192 vs. placebo to be disclosed at presentation).

Intracoronary radiotherapy with Ir-192 plus stenting effectively inhibits luminal renarrowing in pts with restenosis.